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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,785	06/13/2007	Sten Linnarsson	GENI-015/01US 306522-2037	2963

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,785	LINNARSSON, STEN	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/28/09 & 9/22/06* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 7/10/2009 is acknowledged. Claims 1-45 have been canceled. Claims 46-63 have been added. Claims 46-63 are drawn to the elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

2. The disclosure is objected to because of the following informalities:

(a) The disclosure is objected to at pages 34, 36 and 37 because the specification comprise sequences that are not represented by a sequence identifier (SEQ ID NO:). It is suggested amending the disclosure to recited an appropriate sequence identifier, SEQ ID NO:.

Claim Objections

3. Claim 61 is objected to because of the following informalities: Claims 61 is objected because of improper claim construction. It is suggested inserting --wherein said oligonucleotide is-- after, "claim 60," to clarify what reference is being made to.. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 46-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The claims 46-63 are indefinite and confusing in the claim 46 because the claims do not provide a clear nexus between the steps such that a clear interpretation of Applicant's intent can be ascertained. Specifically, the claims do not provide a clear nexus as to how the target sequence of the DNA sample is provided. There appear to be a gap in the steps because the claims appear to suggest that the DNA sample provided is engineered to contain a rolling circle amplification primer annealing sequence and target fragments from a shotgun library. However, the claims do not provide any steps for engineering the DNA samples or for obtaining fragments from a shotgun library. Given the gap between the steps, it cannot clearly be determined how one is to provide the DNA sample as claimed. It is noted that while minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion (see *ex parte Erlich*, 3 UsPQ2d1011, p.1011 (Bd. Pat, Applicant. Int.1986). It is further noted that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Clarification is required as to Applicant's intent.

(b) Claims 48-50 are indefinite and confusing at "effective specificity of 3 to 10 bases" because the term has not bee adequately defined in the instant specification or claims and it cannot be determined what is meant by effective specificity in reference to the number of bases as currently claimed. The limitation is confusing in the context of the claims.

(c) Claim 60 is indefinite and confusing at "said oligonucleotide is stabilized" because it cannot be determined how the limitation "stabilized" is intended to limit or define the oligonucleotide. It is unclear if Applicant is suggesting that the oligonucleotide is stabilized to the surface of the array, or is designed or isolated in a specific manner or something entirely different. In any case, the terminology is confusing in the claims as currently written.

(d) Claims 57-58 are indefinite for the recitation of "10% CV" and "5% CV" because it is unclear as to what is meant by the terms 10% CV and 5% CV in terms of the length of the target sequence. Clarification is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Note* Given the ambiguity of the claims as noted above, the claims are given the broadest reasonable interpretation by the Examiner for the purpose of application of prior art.

7. Claims 46, 47, 59 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rothberg et al (US 6274320, August 2001) in view of Gunderson et al (US 20050100893 and further in view of Swanson et al (Sensors and Actuators B, vol. 64, pages 22-30, 2000). Regarding claim 46, Rothberg et al teach a method of sequencing comprising providing a plurality of single stranded circular template comprising target sequence and primer binding (annealing) sequence sites (see col. 9, lines 24 to col. 10, line 31) and performing rolling circle amplification to produce rolling circle amplification (RCA) products (col. 11). Rothberg teaches wherein a solid support matrix can be associated with the rolling circle synthesis reaction such that signals are generated onto a glass source (see col. 13, lines 27-56). Rothberg teaches multiple oligonucleotides may be attached to a solid support for subsequent sequencing analysis of a desired target (see col. 9, lines 16-24).

Rothberg et al do not expressly teach that the rolling circle amplification products are randomly immobilized on a solid support followed by sequential hybridization and analysis using field programmable gate array.

Gunderson et al teach detection of nucleic acid amplification products, including RCA products using bead arrays (0122). Gunderson et al teach that rolling circle amplification products can be easily detected by hybridization to probes in a solid phase format (e.g., an array of beads). Gunderson et al teach that an additional advantage of

the RCA is that it provides the capability of multiplex analysis in parallel. Gunderson et al teach that by combining the sensitivity of RCA and parallel detection on arrays, many sequences can be analyzed directly from genomic DNA (0204). Gunderson et al teach that various hybridization methods can be used for analysis on an array. For example, Gunderson teaches that their method for sequencing comprises detecting mismatches against a standard (see 0295). Gunderson et al also teaches that plurality of probes (panel of probes) can be used as "readout probes" for detecting mismatches in sequences (0296 and 0537). Gunderson et al teach that random arrays may be used in the method (0424 and 0567) and further teaches wherein sequence analysis may be performed using sequential hybridization on the arrays (see 0609). Gunderson et al also teaches obtaining spectral data using specific tags (0316 and 0450).

Neither Rothberg et al nor Gunderson et al teach further analysis of the amplification products using field programmable gate array. However, this technique is known in the art.

For example, Swanson et al teach a DNA hybridization assay on a biochip, wherein said chip is assessed by a single-board control circuit based on a field programmable gate array (FPGA) (see abstract and section 3, especially page 28). Swanson et al teach that the FPGA board incorporates the necessary hardware and software to control all the hybridization chip functions as well as to drive associated pumps and optical components that are used to read out the fluorescence signal from the chip. Swanson et al teaches that in addition, the instrument interfaces with the PC to allow control by means of a graphical user interface and provide for data analysis

(col. 1, lines 3-10 of page 23). Swanson et al teach that the FPGA is programmed to handle all the necessary logic function to control the chip (section 2.2 at page 25). Swanson et al teach that the biochip allows for analysis of a large number of samples with increase sensitivity under electronic control

One of ordinary skill in the art at the time of the claimed invention would have been motivated to incorporate sequential hybridization on an array and spectral analysis of using FPGA as taught by Gunderson et al in view of Swanson et al in to the rolling circle sequencing method of Rothberg for detection of mutated sequences, as a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. In turn, because the use of hybridization biochips controlled by FPGA for spectral analysis allows for full electronic control and high sensitivity, one of ordinary skill would have been motivated for the benefit of improving means of determining the sequence of a target. The ordinary artisan would have been motivated to analyze rolling circle amplification products on the hybridization biochip as taught by Gunderson in view of Swanson et al based on the teaching of Rothberg that the use of rolling circle amplification allows for the determination of nucleic acid sequence information without the need for first cloning the nucleic acid sequence (Rothberg, col. 5, lines 29-31). Rothberg et al additionally teaches that the method is useful for detecting single nucleotide polymorphism as well as sequencing of artificial sequences (see col. 5, lines 31-33). One of ordinary skill in the art at the time of the claimed invention could expect a reasonable expectation of success in performing the sequencing method of Rothberg et al in view of Gunderson et al in view of Swanson et al, since Gunderson et al teach

substitution of various techniques including rolling circle amplification, use of random arrays and sequential hybridization of means of sequencing a desired target.

Prior art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ladner (citation made of record in IDS) teach a method of rolling circle and PCR ligation and hybridization on a universal probe array (abstract).

Conclusion

No claims are allowed. However, some of the claims have not been rejected under prior art. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Examiner, Art Unit 1637